Sigma factors

Many different Sigma factors.

Table 8.2 Sigma factors in *Escherichia coli*

Name[a]	Upstream (−35) Consensus Recognition Sequence[b]	Function
σ^{70}	TTGACA	For most genes, major sigma factor during normal growth
σ^{54}	TTGGCACA	Nitrogen assimilation
σ^{38}	CCGGCG	Major sigma factor during stationary phase, also for genes involved in oxidative and osmotic responses
σ^{32}	TNTCNCCTTGAA[c]	Heat shock response
σ^{28}	TAAA	For genes involved in flagella synthesis
σ^{24}	GAACTT	Response to misfolded proteins in periplasm
σ^{19}	AAGGAAAAT	For certain genes in iron transport

Cold Shock

Triggered by a sudden drop in temperature. Specific Sigma factor SigmaL, increases. Results in the increased expression of helicases, nucleases and ribosomal proteins.

Protects nucleic acid from adverse temperatures by wrapping around the DNA.

Starvation and RpoS

Bacteria will often live in variable nutrient conditions. Transition from Log to stationary phase often.

RpoS is associated with various stress conditions, heat, acid, salt conc and oxidative stress.

It is the central regulator which switches on genes required for survival in these conditions. It switches on the genes required for said conditions and off the genes which are non-essential.

Regina Hengay found that stationary phase will start much earlier than previously thought so there are still enough nutrients to survive on.

During rapid growth, translation is inhibited and RpoS is degraded, but once entry into the stationary phase the gene is upregulated.

As (p)ppGpp increases in response to starvation it

-Promotes an increase RpoS transcription

-Promotes increased RpoS translation

-Inhibits degradation

-improved activity of RpoS

Over 60 genes are transcribed once RpoS has been translated into a protein some are involved in the cell wall maintenance.

Temp and gene expression

The change of temperature from 0 -25°C to a human internal temperature 37°C is a trigger for bacteria.

This change results in changes in DNA supercoiling at the promoters, this isn't under the effect of gyrase and isomerase.

Instead it is controlled by global regulators (Nucleotide-associated proteins) of which there at least 12 such proteins in E. coli. Examples are FIS (factor for inversion Stimulated and H-NS (Histone-like Nucleoid Structuring Protein).

These effect DNA topology at the promoter and therefore effect transcription.

Supercoiling works by changing the distance between the -35 sequnce and the prinbow box.

Salmonella use this technique to switch between different types of the protein flagellin. As a result, flagella with different structures are assembled. Once an adaptive response has been mounted against one type of flagellin, or if a previous encounter has left the adaptive immune system ready to deal with one type of flagellin, switching types renders previously high affinity antibodies, TCRs and BCRs ineffective against the flagella.

Phase variation can occur in two ways:

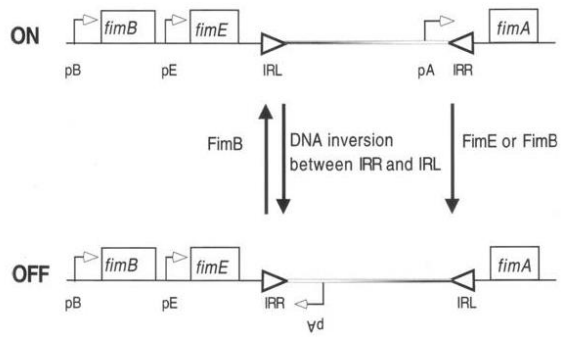
Site-specific Inversion

Through the utilisation of recombinases and IS sequences. When inverted the gene will be switched off and be unable to be read.

In E.coli this occurs with the gene for pilin, S. typhimurium this effects the expression of multiple genes for flagellin.

FimA – E.coli

Phase variation – Site specific inversion



Phase variation – site specific inversion. pB, pE and pA are promoters for the genes *fimB, fimE* and *fimA* respectively. IRL and IRR are inverted repeats. FimB and FimE are recombinases that bind to the inverted triangles IRL an IRR. The result is an inversion of the DNA sequence (shaded bar) that turns ON or OFF the transcription of *fimA*.

This depends on the stage of infection.

Insertion and excision

If excision is precise and the original DNA sequence is restored. Reversible phase variable can be mediated by transposition. Phase variation mediated by transposition targets specific DNA sequences.

Pseudomonas atlantica contains a keps locus which encodes for extra cellular polysaccharides and the on off expression is controlled by the absence of IS-492. When excised the IS element becomes circularised and the gene switched on.

Gene conversion

Gene conversion is where there are several copies of a gene encoding for something like pili (N. gonorrhoea) and the silent genes (PilS, not being used) can recombine into the active pilin gene (PilE) and produce a new phenotype.

Epigenetic Modificaiton

Doesn't change sequence but methylates sequences and alters the binging of transcriptional factors

AG43 – e. coli.

Nested DNA inversion

C. fetus surface proteins where the promoter can shift between copies of the gene and allow the transcription of a different gene.

Slip strand

Can occur during replication or repair of DNA, where to many or not enough nucleotides are added/taken from the promoter, this stops the site from being read by the RNA polymerase.

Listeria

internalised into cell via InlA of InlB (Internalin, which are also adhesins) pathways

A relies on the interaction of A and surface protein E-Cadherin (only expressed on epithelial cells) which activates catenin (a protein which interacts with actin) and Rho GTPase to rearrage the cytoskeleton.

B binds to the host surface protein Met (a ubiquitously expressed protein) which activated PI3K an ezyme which catalyses the degredation of actin as well as Rho GTPase which rearranges the actin for depolymerisation.

Once in the cell the organism will produce listeriolysin to rupture it. Forms pores.

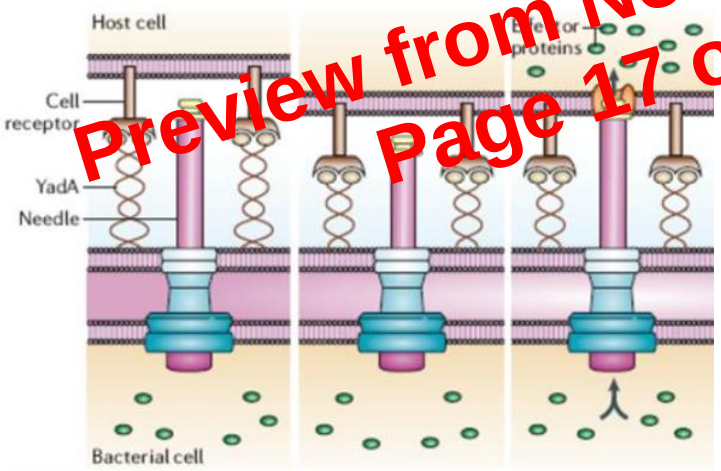
The organism will replicate in the cytosol of the host cell and eventually use actA to accumulate f-actin behind the cell and force it through the cell membrane into an adjacent cell (where it will now have two membranes which are then "popped" by listeriolysin.

T3SS only found in Gram Negative organisms

Associated with PathoIslands, con be on the plasmid or chromosome, encodes for a specialised secretion system.as well as effector molecules.

These systems are highly similar to each other and to flagella (they just miss the Mot proteins, C-ring and hook proteins).

Required direct contact, once bound the plug on the end of the T3SS is released and the genes encoding for effects are expressed. These effects can create pores in the host cell so that the needle can enter the cell wall and inject effector proteins.



The effectors attack host cell signalling pathways or host cell transcription.

Overall there is a very varied effect on the host cell.

EPEC/EHEC – actin rearrangement

Yersina – Macrophage survival and apoptosis

Salmonella – Membrane disruption, invasion, prevention of lysosome formation.

EPEC and EHEC form pedestals to push the organism into the intestinal lumen for better acquisition of nutrients.

EspB and D are injected into the host cell via EspA, once the pore has formed Tir protein moved through and fits its self into the cell membrane, a portion of this protein sticks out of the membrane and binds with high affinity to the corresponding protein (intimin) on the E. coli cell surface. The Tir Protein then becomes phosphorylated.

Once phosphorylated Tir which is also a Receptor Tyrosine Kinase (RTK) activates condensation (cofilin) and polymerization (profilin) of actin filaments under the bacterial cell to form a pedestal.